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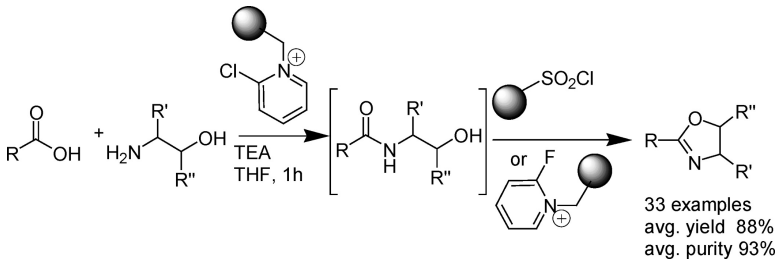

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A Straightforward, One-Pot Protocol for the Preparation of Libraries of 2-Oxazolines

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A practical protocol for the parallel synthesis of 2-oxazolines using polymer-supported reagents is described. Polymer-supported Mukaiyama reagent is used to couple a carboxylic acid with an amino alcohol, giving a β-hydroxyamide, which is then cyclized in situ using either polymer-supported sulfonyl chloride resin or polymer-bound 2-fluoropyridinium triflate. Both 2,4-disubstituted and 2,4,5-trisubstituted 2-oxazolines are obtained in high yields and excellent purities after a simple resin filtration and solvent evaporation routine.

Introduction

Among heterocycles, 2-oxazolines have attracted a lot of interest due to the biological activity displayed by many molecules possessing this core structure (Figure 1). 2-Indolyloxazolines are potent tubulin polymerization inhibitors, with a potential application as orally active anticancer agents.[1] D-Fluviabactin, the unnatural enantiomer of a microbial iron chelator, has been described as a potent agent for clearing iron from animals in a model of iron overload in chronically transfused thalassemia patients.[2] Deflazacor, a corticosteroid derivative, has been launched (under the commercial names of Dezacor, Flantadin, and Lantadin) for treatment of different inflammatory conditions.[3] L-161,240 has been described as a potent antibacterial agent, with a MIC (minimal inhibitory concentration) in the same range of other clinically relevant antibiotics, such as ampicillin or rifampicin, and with a mechanism of action based on the inhibition of the biosynthesis of lipid A, the principal constituent of the outer membrane of Gram-negative bacteria.[4] Finally, several 2-oxazolines are known as potent pesticides.[5] In addition, 2-oxazolines have also been described as potential prodrug precursors of carboxylic acids.[6]

Not surprisingly, the high interest for this class of molecules has led to the development of numerous synthetic strategies for their preparation. One of the most common routes involves the preparation of β-hydroxyamides followed by cyclization. This last step can be performed using a variety of reagents, including Burgess reagent,[7] DAST,[8] PPh_3-DIAD[9] and DIC-Cu$(OTf)_2$.[10]

To facilitate the preparation of the large number of 2-oxazolines needed for biological screenings, some methodologies have also been described that do not require purification of the heterocyclic product and are, as such, suitable for parallel synthesis: Wipf has described the preparation of oxazolines using a boronic acid catalyst;[11] Pirrung used a catch-and-release approach using a polymer-supported tosyl chloride equivalent.[12]

Because of the pharmacological interest in these molecules, we became interested in the preparation of solution-phase, focused libraries of druglike 2-oxazolines. Among the methods reported in the literature, the method based on polymer-supported tosyl chloride seemed the most attractive, especially in terms of purity of the final compounds. However, from our point of view, it also presented several disadvantages: in the first place, the catch-and-release approach requires three separate steps to be performed, with isolation of the intermediate resin-bound tosylate. This both limits the yields, which are generally lower than 60% and can be as low as 32%, and makes library preparation more tedious and time-consuming. Moreover, the acyl chlorides needed as building blocks are more expensive, less stable, and less available than the corresponding carboxylic acids ($\sim$1000 compounds as compared to $>$40 000 in the ACD database). A methodology employing the latter would be much more advantageous and would increase the chemical diversity accessible for the library. As an example, 796 carboxylic acids containing a 4-pyridinecarboxylic acid substructure are reported in the ACD database (1943 in the SciFinder database), as compared to only 8 acyl chlorides (10 in the SciFinder database).

Recently, we have developed polymer-supported 2-chloro-*N*-pyridinium triflate **1a**, an insoluble version of the popular Mukaiyama reagent.[13] We have demonstrated that this reagent is very efficient at promoting the coupling of carboxylic acids with either amines or alcohols, giving amides or esters, respectively, in high yields and purities without the need for chromatography or crystallization. In addition to this, the preparation of the reagent is very straightforward, requiring only one operationally simple step from commercially available 4-hydroxymethylphenoxymethyl polystyrene (Scheme 1).

During our evaluation of the reagent, we were surprised to find that, even if the reagent can very efficiently promote esterification reactions in short reaction times, treating an amino alcohol with 1 equiv of a carboxylic acid resulted in the completely chemoselective formation of the correspond-

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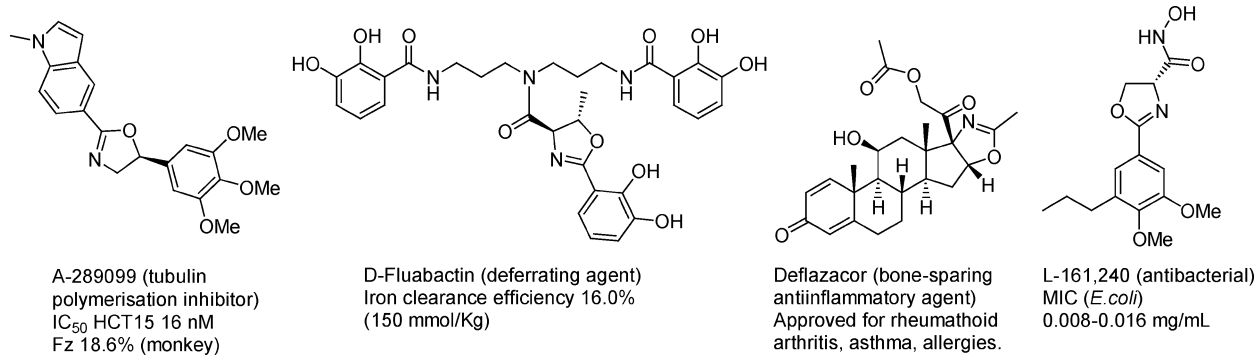
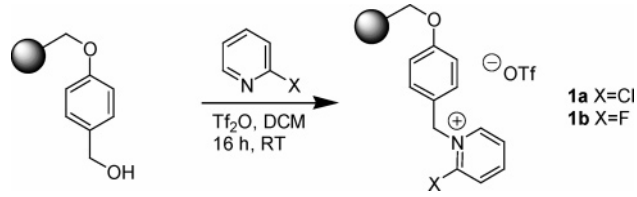
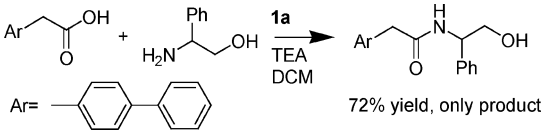


Figure 1. Some biologically active molecules possessing a 2-oxazolinic core.

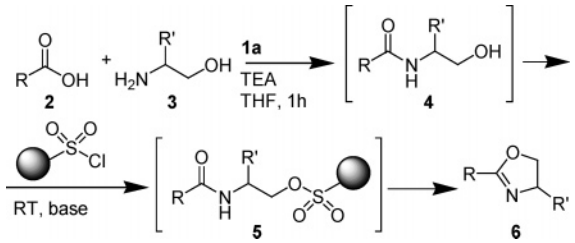
Scheme 1. Synthesis of Polymer-Supported Reagents **1a** and **1b**



Scheme 2. Chemoselective Amide Synthesis Using Reagent **1a**



Scheme 3. Proposed Synthesis of 2-Oxazolines



ing β-hydroxy amide (Scheme 2). This chemoselectivity is achieved without the need for slow addition of the carboxylic acid or temperature control: the carboxylic acid and the amino alcohol can be simply mixed together, followed by addition of the resin at room temperature, making this very simple procedure very suitable for applications in parallel chemistry.

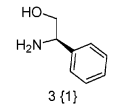
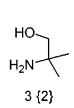
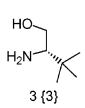
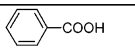
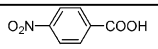
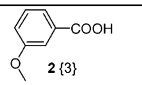
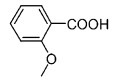
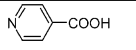
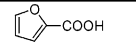
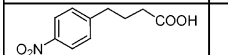
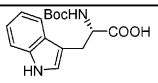
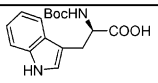
At this point, we became interested in incorporating this reaction in a synthetic methodology for the synthesis of libraries of 2-oxazolines, which would be more high yielding and simpler to implement than the reported methodology, while also using carboxylic acids rather than acyl chlorides for introducing diversity.

Results and Discussion

The envisioned sequence is depicted in Scheme 3; the carboxylic acid and amino alcohol would be reacted using **1a**. Without isolation of the intermediate β-hydroxyamide **4**, tosyl chloride resin would be added to generate the polymer-bound reactive intermediate **5**, which would immediately cyclize to release the desired product. It was assumed that the initial coupling would proceed cleanly enough to grant a good purity of the final compounds without the need to isolate intermediate **5**. This would both give higher yields compared to the literature procedure (the low yields being caused by premature cyclization before isolation of **5**) and greatly simplify the procedures for the generation of the library.

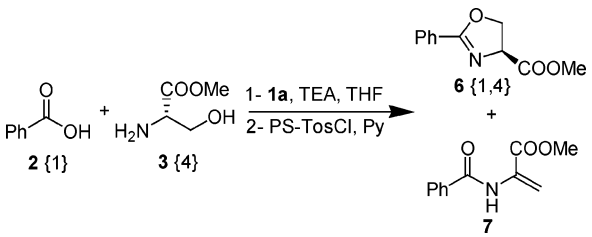
The results obtained for a small sample library are summarized in Table 1. The products were generally obtained

Table 1. Synthesis of 2-Oxazolines Using **1a** and Polymer-Supported Tosyl Chloride

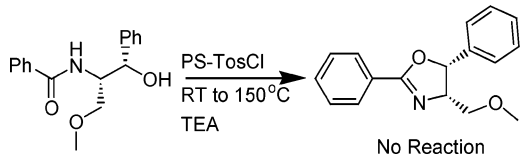
	 3 {1}	 3 {2}	 3 {3}
 **2** {1}	93%[a] (99%)[b]	93% (96%)	97% (98%)
 **2** {2}	87% (92%)	98% (98%)	95% (97%)
 **2** {3}	90% (89%)	99% (93%)	92% (97%)
 **2** {4}	89% (97%)	98% (90%)	96% (96%)
 **2** {5}	98% (96%)	79% (92%)	86% (95%)
 **2** {6}	98% (96%)	97% (96%)	91% (97%)
 **2** {7}	91% (87%)	89% (94%)	94% (91%)
 **2** {8}	69%[c] (90%)[c]	67% (95%)	76%[c] (88%)[c]
 **2** {9}	83%[c] (94%)[c]	56% (89%)	77%[c] (87%)[c]

[a] Isolated yield. [b] Purity (HPLC and ^{1}H NMR). [c] Sum of both diastereoisomers.

Scheme 4. Attempted Preparation of Oxazolines Derived from Serine Methyl Ester



Scheme 5. Failed Attempts at the Preparation of a 2,4,5-trisubstituted Oxazoline



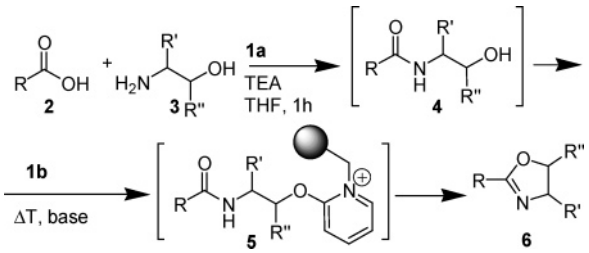
with high purity and with high yield, usually above 90%. Electron-rich and electron-poor aromatic carboxylic acids, as well as different heteroaromatic carboxylic acids, could all be reacted with equally excellent results, although electron-donating substituents and electron-rich heteroaromatics displayed slightly slower kinetics. Ortho substitution seems to have a negative effect on the kinetics of the reaction. Aliphatic carboxylic acids could be used, as well, with good success, although the purities were somewhat lower. When α-chiral carboxylic acids were employed, the configuration of the chiral center was well-maintained: only 3% of racemization was observed when either enantiomer of Boc-tryptophan was reacted with (*R*)-2-phenyl-2-aminoethanol **3**{*1*} (measured by ^{1}H NMR). A similar value (2% racemization) could be observed when (S)-*tert*-leucinol **3**{*3*} was used.

Very importantly, the workup was very simple and easy to apply to parallel chemistry: a filtration on an amino-functionalized solid-phase extraction plug, followed by washing with DCM and solvent evaporation afforded the products in high purity (HPLC, HPLC/MS, and NMR).

A substantial concentration of base (10−25% v/v) is necessary to achieve the cyclization. However, using more than 5−10 equiv of TEA during the acylation step lead to decreased purity of the final compounds. As such, 3 equiv of TEA was used for the first part of the reaction, and an additional quantity of base was added for the subsequent cyclization. Both pyridine and triethylamine were used for this step, the latter being necessary for products derived from aliphatic carboxylic acids or electron-rich aromatic systems. In fact, cyclization of the hydroxyamides derived from phenylglycinol **3**{*1*} and 2-methoxybenzoic acid **2**{*4*}, 3-(4-nitrophenyl)-butyric acid **2**{*7*} or Boc-tryptophan **2**{*8*} gave incomplete conversions after 4 days of reaction when pyridine was used as base, but cyclized more readily in the presence of TEA. As a result, the use of TEA is recommended for library generation. In addition, the use of TEA rather than pyridine for the acylation step is essential, because no hydroxyamide formation could be observed when benzoic acid and phenylglycinol were treated with **1a** and pyridine.

To ensure that the first step of the reaction proceeded with complete chemoselectivity, without formation of bis-acylated

Scheme 6. Preparation of 2,4,5-Trisubstituted Oxazolines

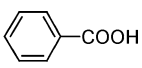
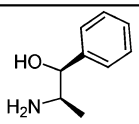
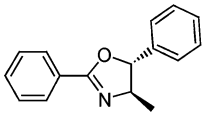
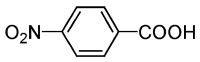
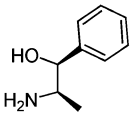
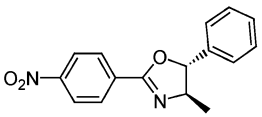
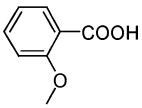
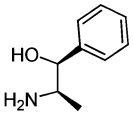
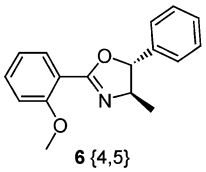
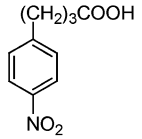
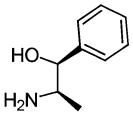
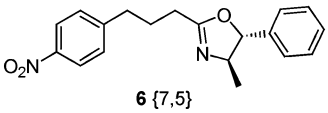
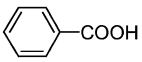
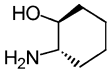
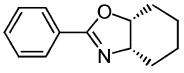
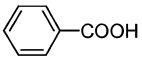
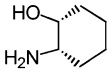
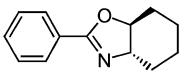
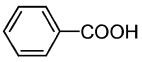
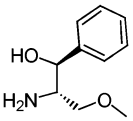
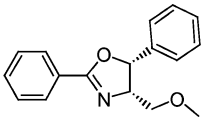
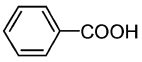
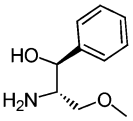
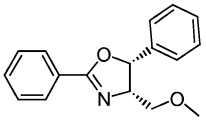


products, a slight excess (1.2 equiv) of the amino alcohol component was used, the excess reagent being effectively scavenged by the same tosyl chloride resin used to accomplish the cyclization. THF was selected as solvent to achieve a better solubility of the intermediate hydroxyamide while still allowing good swelling of the resin and easy removal after the reaction. In some cases, the initial mixture of amino alcohol and carboxylic acid gave a precipitate; however, this did not hinder the acylation step (the precipitate gradually dissolving upon reaction) and did not cause any problems regarding either the chemoselectivity or the yield of the reaction.

When serine methyl ester **3**{*4*} was employed as the aminolcohol, a consistent amount (from 10 to 20 mol %, depending on reaction conditions) of dehydroalanine derivative could be observed (Scheme 4). Reports in the literature indicate that dehydration to form this unwanted byproduct is normally suppressed by using a weak base, such as pyridine, rather than TEA.[12a] The standard conditions used for the products in Table 1 called for the use of 3 equiv of TEA during the acylation step, followed by addition of a second aliquot of base (pyridine or TEA) together with the sulfonyl chloride resin. These conditions, when applied for the serine derivative, led to formation of ∼20 mol % of dehydroalanine derivative. When pyridine was used as base also for the first step, none of the desired intermediate hydroxyamide was formed. In this case, the possibility to independently modulate the reaction conditions for both the acylation and cyclization steps, which is granted by adoption of the "catch-and release" methodology, represents an advantage.

Although the use of polymer-supported tosyl chloride could afford excellent results for the preparation of 2,4-disubsituted 2-oxazolines, it still had one significant weakness: as reported by Pirrung,[12a] cyclization of hydroxyamides substituted α to the hydroxy function could not be achieved except when the substituent was a mere methyl group, as anything bulkier would prevent the tosylation step. For example, several experiments were performed, employing different bases, from room temperature up to 150 °C in a microwave reactor, but we were unable to achieve the cyclization of the amide derived from (*S*,*S*)-2-amino-3-methoxy-1-phenyl-propan-1-ol **3**{*8*} and benzoic acid to the corresponding 2,4,5-trisubstituted-2-oxazoline (Scheme 5). Because many pharmacologically interesting oxazolines present substituents in the 5- position (see examples in Figure 1), we decided to investigate whether a suitable methodology for the preparation solution-phase libraries of such compounds could be developed.

Table 2. Synthesis of 2,4,5-Trisubstituted Oxazolines

Entry	Acid	Aminoalcohol	Oxazoline	Yield (%)[a]	Purity (%)[b]	Cis/Trans ratio[b]
1	 **2** {1}	 **3** {5}	 **6** {1,5}	90	95	<5 : >95
2	 **2** {2}	 **3** {5}	 **6** {2,5}	94	87	<5 : >95
3	 **2** {4}	 **3** {5}	 **6** {4,5}	91	96	<5 : >95
4	 **2** {7}	 **3** {5}	 **6** {7,5}	98	95	<5 : >95
5	 **2** {1}	 **3** {6}	 **6** {1,6}	79	90	>95 : <5
6	 **2** {1}	 **3** {7}	 **6** {1,7}	No Rxn.	--	--
7	 **2** {1}	 **3** {8}	 **6** {1,8}	82[c]	89[c]	5 : 1
8	 **2** {1}	 **3** {8}	 **6** {1,8}	77[c, d]	89[c, e]	97 : 3

[a] Isolated yield. [b] HPLC and ^{1}H NMR. [c] Sum of both diastereoisomers. [d] Reaction run at room temperature. [e] 7 mol % of uncyclized amide present (evaluated by ^{1}H NMR).

It is known in the literature that analogues of Mukaiyama reagent bearing a fluorine instead of a chlorine atom in the 2- position can react with alcohols and activate them toward attack by nucleophiles. Because we had easy access to polymer-supported derivative **1b** through the same methodology employed to prepare **1a**, we decided to test whether **1b** could promote the cyclization of β-hydroxyamides (Scheme 6). Very interestingly, we found that **1b** can promote the formation of 2,4,5-trisubstituted 2-oxazolines quite readily (Table 2). In contrast, when only **1a** was employed, no trace of cyclization could be observed. To the best of our knowledge, the use of 2-halopyridinium salts to promote the cyclization of β-hydroxyamides does not have precedents in the literature. By giving easy access to 5-substituted 2-oxazolines, this reaction allows the introduction of an extra diversity point in 2-oxazoline libraries, which could not be exploited with the methodologies currently available for solution-phase parallel chemistry.

Generally, the reaction was complete within 10 min at 120 °C under microwave irradiation, and we found that stirring the mixture for 1 h at room temperature before beginning the microwave irradiation could be advantageous. Reactions run at room temperature required 2−3 days to achieve >90% conversion, but complete disappearance of the intermediate hydroxyamide could never be achieved. As before, the workup consisted only in filtration of the resin on an amino functionalized polymer plug, followed by evaporation of the solvent.

Both electron-poor and electron-rich aromatic acids, with ortho or para substitution, as well as aliphatic carboxylic acids could be used without significant difference of reactivity under the conditions employed (similar yields and purities). The reaction proceeds with inversion of configuration at the 5 position, which points toward an S_N2 mechanism. Products derived from (1*S*,2*R*)-norephedrine **3**{*5*} were converted to the corresponding trans oxazolines (Table 2, entries 1−4). Trans 2-amino-1-cyclohexanol **3**{*6*} could be converted to the desired cis oxazoline (entry 5) with good yield and complete diastereoselectivity (NMR and GC/MS), but cis 2-amino-1-cyclohexanol **3**{*7*}, for which a S_N2 substitution is conformationally much more difficult, could not be converted into the corresponding trans oxazoline (entry 6). A lower diastereoselectivity was observed with the oxazoline derived from (*S*,*S*)-2-amino-3-methoxy-1-phenyl-1-propanol **3**{*8*} (entry 7), and the presence of the phenyl substituent stabilizes a possible carbocation intermediate, partially enabling an S_N1 pathway, which leads to the more stable *trans*-oxazoline. However, even under these conditions and at high temperature, the expected *cis*-oxazoline arising from the S_N2 pathway is predominantly formed. Performing the reaction at room temperature (entry 8) increases the diastereomeric excess to a very gratifying 94%, albeit with longer reaction times (3 days, 7 mol % of uncyclized product was still present in the final product).

Conclusions

A straightforward protocol for the preparation of solution-phase libraries of 2-oxazolines combining a chemoselective acylation step using polymer-supported Mukaiyama reagent followed by cyclization using polymer-supported tosyl chloride or polymer-supported 2-fluoropyridinium triflate has been developed. The reaction is one-pot and operationally simple and gives products in high yields and purities. Polymer-supported tosyl chloride is the reagent of choice for the preparation of libraries of 5-unsubstituted oxazolines due to the robustness of the method and the fact that this reagent is commercially available. On the other hand, the use of polymer-supported 2-fluoropyridinium triflate allows for the preparation of 5-substituted oxazolines so that an extra point of diversity can be introduced. Because the reaction proceeds almost exclusively with inversion of configuration, diastereomerically pure compounds are obtained, which ensures the homogeneity of the library.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were recorded using a Bruker DPX-300 spectrometer (300 and 75.47 MHz, respectively). HPLC analysis was performed on a Waters 2695 instrument equipped with a Waters 996 photodiode array detector using an XTerra MSC8 3.5 4.6 μm × 50 mm column. **Chromatographic Conditions.** Method A: gradient from 95% H_2O (0.1% TFA)/5% CH_3CN (0.1% TFA) to 5% H_2O (0.1% TFA)/95% CH_3CN (0.1% TFA) over 8 min, flow 2 mL/min. Method B: gradient from 95% H_2O/5% CH_3CN to 5% H_2O/95% CH_3CN over 8 min, flow 2 mL/min. Mass spectra were determined on a Micromass ZMD (electrospray, positive or negative ionization). All reagents were purchased and used without further purification. Microwave-assisted reactions were performed on a Smith synthesizer. Wang resin (4-hydroxymethylphenoxymethyl polystyrene, cross-linked with 1% divinylbenzene, 150−300 μm, loading 1.7 mmol/g, Part no. 1463-4689, batch Wang 073) was purchased from Polymer Laboratories. (Polystyrene)tosyl chloride HL (110 μm, loading 2.82 mmol/g, Part no. 800365, batch 02631) was purchased from Argonaut. The amino-functionalized SPE columns were Isolute NH_2 SPE column, 2 g, Part no. 470-0200-D. All other reagents were bought from Aldrich and used without purification. Anhydrous solvents were purchased, stored on molecular sieves, and used without prior distillation.

Preparation of Resins 1a and 1b. Wang resin (5.00 g, 8.5 mmol) was suspended in dry DCM (50 mL). Either 2-chloropyridine (4.0 mL, 42 mmol, 5 equiv) or 2-fluoropyridine (3.8 mL, 42 mmol, 5 equiv) was added, and the mixture was cooled with an ice bath. Trifluoromethanesulfonic anhydride (2.0 mL, 12 mmol, 1.4 equiv) was added dropwise, and after 5 min, the ice bath was removed. The mixture was stirred overnight at room temperature. The resin was collected by filtration and washed with DCM, DMF, and DCM and dried under vacuum.

General Procedure for 2-Oxazoline Preparation Using Resin 1a and (Polystyrene)tosyl Chloride. The carboxylic acid **2** (0.15 mmol), amino alcohol **3** (0.18 mmol) and TEA (62 μL, 0.45 mmol) were placed in a vial together with anhydrous THF (3 mL). Resin **1a** (240 mg, 0.30 mmol) was added, and the mixture was stirred vigorously for 1 h. (Polystyrene)tosyl chloride (160 mg, 0.30 mmol) and additional base (pyridine or TEA, 0.3−1 mL, see below) were added, and the mixture was stirred for 16−48 h (see below). The resin was removed by filtration, and the filtrates were passed through an amino-functionalized SPE column (Isolute NH_2 SPE column, 2 g). The resin and SPE column were washed with 15 mL of DCM, then the combined filtrates were evaporated under vacuum to afford the desired 2-oxazolines **6**, which were analyzed without further purification.

(*R*)-2,4-Diphenyl-2-oxazoline 6{*1,1*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of pyridine (0.3 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 7.96 (2H, m), 7.46−7.16 (8H, m), 5.31 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.71 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.19 (1H, t, J = 8.5 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 164.7, 142.3, 131.5, 128.7, 128.4, 128.3, 127.6, 127.5, 126.7, 74.8, 70.1. HPLC t_R = 2.08 min (A). ES-MS m/z 224.3 $(M + H)^+$.

4,4-Dimethyl-2-phenyl-2-oxazoline 6{*1,2*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of pyridine (0.3 mL), reaction time 40 h. ^{1}H NMR ($CDCl_3$) δ_H: 7.86 (2H, m), 7.42−7.29 (3H, m), 4.03 (2H,s), 1.31 (6H, s). ^{13}C NMR ($CDCl_3$) δ_C: 162.0, 131.1, 128.3, 128.2, 128.0, 79.1, 67.5, 28.4. HPLC t_R = 2.63 min (B). ES-MS *m*/*z* 176.4 $(M + H)^+$.

(*S*)-4-*tert*-Butyl-2-phenyl-2-oxazoline 6{*1,3*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of pyridine (0.3 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 7.88 (2H, m), 7.42−7.29 (3H, m), 4.26 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.15 (1H, dd, J = 8.5 Hz, J = 7.5 Hz), 3.97 (1H, dd, J = 10.0 Hz, J = 7.5 Hz), 0.87 (9H, s). ^{13}C NMR ($CDCl_3$) δ_C: 163.2, 131.1, 128.2, 128.0, 76.1, 68.7, 34.0, 25.8. HPLC t_R = 1.73 min (A). ES-MS *m*/*z* 204.4 $(M + H)^+$.

(*R*)-2-(4-Nitrophenyl)-4-phenyl-2-oxazoline 6{*2,1*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of pyridine (0.3 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 8.21 (2H, d, J = 9.0 Hz), 8.14 (2H, d, J = 9.0 Hz), 7.33−7.20 (5H, m), 5.37 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.79 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.27 (1H, t, J = 8.5 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 162.8, 149.6, 141.5, 133.3, 129.5, 128.9, 127.9, 126.7, 123.5, 75.3, 70.4. HPLC t_R = 3.79 min (B). ES-MS *m*/*z* 269.3 $(M + H)^+$.

4,4-Dimethyl-2-(4-nitrophenyl)-2-oxazoline 6{*2,2*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (1 mL), reaction time 40 h. ^{1}H NMR ($CDCl_3$) δ_H: 8.18 (1H, d, J = 8.5 Hz), 8.03 (1H, d, J = 8.5 Hz), 4.09 (2H, s), 1.33 (6H, s). ^{13}C NMR ($CDCl_3$) δ_C: 160.2, 149.3, 133.9, 129.2, 123.4, 79.5, 68.2, 28.3. HPLC t_R = 3.10 min (B). ES-MS *m*/*z* 221.2 $(M + H)^+$.

(*S*)-4-*tert*-Butyl-2-(4-nitrophenyl)-2-oxazoline 6{*2,3*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 8.18 (2H, d, J = 9.0 Hz), 8.05 (2H, d, J = 9.0 Hz), 4.34 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.21 (1H, t, J = 8.5 Hz), 4.03 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 0.88 (9H, s). ^{13}C NMR ($CDCl_3$) δ_C: 161.4, 149.4, 133.7, 129.2, 123.4, 76.5, 69.2, 34.0, 25.8. HPLC t_R = min (3.98). ES-MS *m*/*z* 249.2 $(M + H)^+$.

(*R*)-2-(3-Methoxyphenyl)-4-phenyl-2-oxazoline 6{*3,1*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of pyridine (0.3 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 7.55 (1H, dt, J = 7.5 Hz, J = 1.5 Hz), 7.51 (1H, dd, J = 2.0 Hz, J = 1.5 Hz), 7.32−7.20 (6H, m), 6.98 (1H, ddd, J = 8.0 Hz, J = 2.0 Hz, J = 1.0 Hz), 5.30 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.71 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.20 (1H, t, J = 8.5 Hz), 3.76 (3H, s). ^{13}C NMR ($CDCl_3$) δ_C: 164.7, 159.5, 142.3, 129.4, 128.8, 128.7, 127.6, 126.7, 120.9, 118.4, 112.7, 74.9, 70.1, 55.4. HPLC t_R = 2.44 min (A). ES-MS *m*/*z* 254.2 $(M + H)^+$.

4,4-Dimethyl-2-(3-methoxyphenyl)-2-oxazoline 6{*3,2*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (1 mL), reaction time 40 h. ^{1}H NMR ($CDCl_3$) δ_H: 7.46 (1H, dt, J = 8.0 Hz, J = 1.5 Hz), 7.40 (1H, dd, J = 2.0 Hz, J = 1.5 Hz), 7.24 (1H, t, 7.5 Hz), 6.95 (1H, ddd, J = 8.0 Hz, J = 2.0 Hz, J = 1.0 Hz), 4.06 (2H, s), 3.75 (3H, s), 1.32 (6H, s). ^{13}C NMR ($CDCl_3$) δ_C: 162.2, 159.4, 129.3, 128.9, 120.7, 118.2, 112.5, 79.2, 67.4, 55.4, 28.3. HPLC t_R = 1.40 min (A). ES-MS *m*/*z* 206.4 $(M + H)^+$.

(*S*)-4-*tert*Butyl-2-(3-methoxyphenyl)-2-oxazoline 6{*3,3*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 7.47 (1H, dt, J = 8.0 Hz, J = 1.5 Hz), 7.42 (1H, dd, J = 2.0 Hz, J = 1.5 Hz), 7.23 (1H, t, 7.5 Hz), 6.94 (1H, ddd, J = 8.0 Hz, J = 2.0 Hz, J = 1.0 Hz), 4.26 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.16 (1H, dd, J = 8.5 Hz, J = 7.5 Hz), 3.97 (1H, dd, J = 10.0 Hz, J = 7.5 Hz), 3.77 (3H, s), 0.87 (9H, s). ^{13}C NMR ($CDCl_3$) δ_C: 163.1, 159.4, 129.3, 129.2, 120.7, 117.7, 112.7, 76.1, 68.7, 55.4, 34.0, 25.8. HPLC t_R = 2.02 min (A). ES-MS *m*/*z* 334.3 $(M + H)^+$.

(*R*)-2-(2-Methoxyphenyl)-4-phenyl-2-oxazoline 6{*4,1*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 7.77 (1H, dd, J = 8.0 Hz, J = 1.5 Hz), 7.36 (1H, ddd, J = 8.0 Hz, J = 7.5 Hz, J = 2.0 Hz), 7.30−7.18 (5H, m), 6.92 (2H, dd, J = 7.5 Hz, J = 2.0 Hz), 5.34 (1H, dd, J = 10.0 Hz, J = 8.0 Hz), 4.68 (1H, dd, J = 10.0 Hz, J = 8.0 Hz), 4.16 (1H, t, J = 8.0 Hz), 3.84 (3H, s). ^{13}C NMR ($CDCl_3$) δ_C: 163.7, 158.5, 142.6, 132.4, 131.4, 128.6, 127.4, 126.7, 120.2, 117.0, 111.7, 74.3, 70.2, 56.0. HPLC t_R = 2.05 min (A). ES-MS *m*/*z* 254.3 $(M + H)^+$.

4,4-Dimethyl-2-(2-methoxyphenyl)-2-oxazoline 6{*4,2*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (1 mL), reaction time 40 h. ^{1}H NMR ($CDCl_3$) δ_H: 7.66 (1H, dd, J = 8.0 Hz, J = 1.5 Hz), 7.40 (1H, dt, J = 8.0 Hz, J = 1.5 Hz), 6.92−6.86 (2H, m), 4.03 (2H, s), 3.82 (3H, s), 1.32 (6H, s). ^{13}C NMR ($CDCl_3$) δ_C: 161.3, 158.3, 132.1, 131.3, 120.2, 117.6, 111.7, 79.0, 67.4, 56.1, 28.3. HPLC t_R = 2.59 min (B). ES-MS *m*/*z* 206.4 $(M + H)^+$.

(*S*)-4-*tert*-Butyl-2-(2-methoxyphenyl)-2-oxazoline 6{*4,3*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 40 h. ^{1}H NMR ($CDCl_3$) δ_H: 7.63 (1H, d, J = 8.0 Hz, J = 1.5 Hz), 7.34 (1H, td, J = 8.0 Hz, J = 1.5 Hz), 6.93−6.86 (2H, m), 4.29 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.17 (1H, dd, J = 8.5 Hz, J = 7.5 Hz), 4.01 (1H, dd, J = 10.0 Hz, J = 7.5 Hz), 3.81 (3H, s), 0.90 (3H, s). ^{13}C NMR ($CDCl_3$) δ_C: 162.4, 158.2, 131.9, 131.2, 120.2, 117.8, 111.7, 68.5, 56.0, 34.0, 25.8. HPLC t_R = 1.98 min (A). ES-MS *m*/*z* 234.4 $(M + H)^+$.

(*R*)-4-Phenyl-2-(4-pyridyl)-2-oxazoline 6{*5,1*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of pyridine (0.3 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 9.00 (2H, d, J = 6.0 Hz), 8.13 (1H, d, J = 6.0 Hz), 7.66−7.53 (5H, m), 5.69 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 5.11 (1H, dd, J =

10.0 Hz, J = 8.5 Hz), 4.59 (1H, t, J = 8.5 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 163.0, 150.3, 141.5, 134.9, 128.9, 127.9, 126.7, 122.1, 75.1, 70.2. HPLC t_R = 2.37 min (B). ES-MS m/z 225.3 $(M + H)^+$.

4,4-Dimethyl-2-(4-pyridyl)-2-oxazoline 6{*5,2*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 40 h. The final resin wash was done using a TEA solution in DCM (5 vol %). ^{1}H NMR ($CDCl_3$) δ_H: 7.50 (1H, dd, J = 2.0 Hz, J = 1.0 Hz), 6.91 (1H, dd, J = 3.5 Hz, J = 1.0 Hz), 6.45 (1H, dd, J = 3.5 Hz, J = 2.0 Hz), 4.06 (2H, s), 1.36 (6H, s). ^{13}C NMR ($CDCl_3$) δ_C: 160.3, 150.1, 135.5, 122.0, 79.4, 68.1, 28.3. HPLC t_R = 2.06 min (B). ES-MS m/z 177.3 $(M + H)^+$.

(*S*)-4-*tert*-Butyl-2-(4-pyridyl)-2-oxazoline 6{*5,3*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 8.62 (1H, dt, J = 6.0 Hz), 7.72 (1H, d, J = 6.0 Hz), 4.31 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.19 (1H, t, J = 8.5 Hz), 4.01 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 0.88 (9H, s). ^{13}C NMR ($CDCl_3$) δ_C: 161.5, 150.2, 135.3, 122.0, 76.4, 69.1, 34.0, 25.8. HPLC t_R = 1.51 min (A). ES-MS m/z 305.4 $(M + H)^+$.

(*R*)-2-(2-Furyl)-4-phenyl-2-oxazoline 6{*6,1*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 7.60 (1H, d, J = 1.5 Hz), 7.41−7.28 (5H, m), 7.07 (1H, d, J = 3.5 Hz), 6.55 (1H, dd, J = 3.5 Hz, J = 1.5 Hz), 5.42 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.80 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.29 (1H, t, J = 8.5 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 156.9, 145.4, 142.8, 141.8, 128.7, 127.6, 126.7, 114.8, 111.6, 74.7, 70.0. HPLC t_R = 3.10 min (B). ES-MS m/z 214.3 $(M + H)^+$.

4,4-Dimethyl-2-(2-furyl)-2-oxazoline 6{*6,2*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 40 h. ^{1}H NMR ($CDCl_3$) δ_H: 7.50 (1H, dd, J = 2.0 Hz, J = 1.0 Hz), 6.91 (1H, dd, J = 3.5 Hz, J = 1.0 Hz), 6.45 (1H, dd, J = 3.5 Hz, J = 2.0 Hz), 4.06 (2H, s), 1.36 (6H, s). ^{13}C NMR ($CDCl_3$) δ_C: 154.5, 145.1, 143.0, 114.1, 11.5, 79.2, 67.7, 28.3. HPLC t_R = 1.99 min (B). ES-MS m/z 166.3 $(M + H)^+$.

(*S*)-4-*tert*-Butyl-2-(2-furyl)-2-oxazoline 6{*6,3*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 7.50 (1H, d, J = 2.0 Hz), 6.90 (1H, d, J = 3.5 Hz), 6.44 (1H, dd, J = 3.5 Hz, J = 2.0 Hz), 4.30 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.16 (1H, t, J = 8.5 Hz), 4.02 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 0.92 (9H, s). ^{13}C NMR ($CDCl_3$) δ_C: 155.6, 145.0, 143.0, 114.0, 111.4, 76.3, 68.7, 33.8, 25.9. HPLC t_R = 1.17 min (A). ES-MS m/z 194.4 $(M + H)^+$.

(*R*)-2-(4-Nitrophenylpropyl)-4-phenyl-2-oxazoline 6{*7,1*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 8.16 (2H, d, J = 8.5 Hz), 7.40−7.21 (7H, m), 5.19 (1H, t, J = 8.5 Hz), 4.61 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.10 (1H, t, J = 8.5 Hz), 2.85 (2H, t, J = 7.5 Hz), 2.44 (2H, t, J = 7.5 Hz), 2.09 (2H, quintet, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 167.9, 149.3, 146.5, 142.3, 129.3, 128.7, 127.6, 126.5, 123.7, 74.5, 69.6, 35.1, 27.3, 27.1. HPLC t_R = 2.68 min (A). ES-MS m/z 311.3 $(M + H)^+$.

4,4-Dimethyl-2-(4-nitrophenylpropyl)-2-oxazoline 6{*7,2*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 40 h. ^{1}H NMR ($CDCl_3$) δ_H: 8.10 (2H, d, J = 8.5 Hz), 7.31 (2H, d, J = 8.5 Hz), 5.14 (2H, t, J = 8.5 Hz), 3.87 (2H, s), 2.74 (2H, t, J = 7.5 Hz), 2.25 (2H, t, J = 7.5 Hz), 1.95 (2H, quintet, J = 7.5 Hz), 1.23 (6H, s). ^{13}C NMR ($CDCl_3$) δ_C: 165.1, 149.4, 146.4, 129.3, 123.6, 78.9, 66.9, 34.9, 28.4, 27.3, 27.1. HPLC t_R = 3.74 min (B). ES-MS m/z 263.4 $(M + H)^+$.

(*S*)-4-*tert*-Butyl-2-(4-nitrophenylpropyl)-2-oxazoline 6{*7,3*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 40 h. ^{1}H NMR ($CDCl_3$) δ_H: 8.11 (2H, d, J = 8.5 Hz), 7.31 (2H, d, J = 8.5 Hz), 4.12 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.00 (1H, t, J = 8.5 Hz), 3.80 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 2.76 (2H, t, J = 8.0 Hz), 2.30 (2H, t, J = 8.0 Hz), 1.95 (2H, quintet, J = 8.0 Hz), 0.86 (9H, s). ^{13}C NMR ($CDCl_3$) δ_C: 166.5, 149.5, 146.4, 129.2, 123.6, 75.7, 68.4, 35.1, 33.5, 27.4, 27.3. HPLC t_R = 2.42 min (A). ES-MS m/z 291.4 $(M + H)^+$.

(1*S*,4′*R*)-[2-(1*H*-Indol-3-yl)-1-(4-phenyl-2-oxazolin-2-yl)-ethyl]-carbamic Acid *tert*-Butyl Ester 6{*8,1*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 8.27 (1H, bs), 7.61 (1H, d, J = 7.5 Hz), 7.36 (1H, d, J = 7.5 Hz), 7.20−7.02 (6H, m), 6.98 (1H, d, J = 2.5 Hz), 6.53 (1H, d, J = 7.0 Hz), 5.48 (1H, d, J = 7.0 Hz), 5.00 (1H, t, J = 10.0 Hz), 4.80 (1H, m), 4.60 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 3.92 (1H, t, J = 8.5 Hz), 3.37 (2H, d, J = 4.0 Hz), 1.43 (9H, s). ^{13}C NMR ($CDCl_3$) δ_C: 167.6, 155.0, 141.4, 136.0, 128.5, 128.0, 127.4, 126.6, 123.1, 122.0, 119.6, 119.0, 111.0, 110.1, 79.6, 75.6, 69.3, 49.7, 28.4, 27.8. HPLC t_R = 2.98 min (A). ES-MS m/z 406.3 $(M + H)^+$.

(1*S*)-[2-(1*H*-Indol-3-yl)-1-(4,4-dimethyl-2-oxazolin-2-yl)-ethyl]-carbamic Acid *tert*-Butyl Ester 6{*8,2*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (1 mL), reaction time 40 h. ^{1}H NMR ($CDCl_3$) δ_H: 8.19 (1H, bs), 7.56 (1H, d, J = 7.5 Hz), 7.30 (1H, d, J = 7.5 Hz), 7.17−7.04 (6H, m), 6.96 (1H, s), 5.22 (1H, d, J = 7.0 Hz), 4.64 (1H, m), 3.91 (1H, d, J = 8.0 Hz), 3.85 (1H, d, J = 8.0 Hz), 3.26 (2H, m), 1.41 (9H, s), 1.12 (3H, s), 0.89 (3H, s). ^{13}C NMR ($CDCl_3$) δ_C: 164.7, 155.0, 136.0, 128.0, 122.0, 121.8, 119.3, 118.9, 111.0, 110.2, 79.5, 66.9, 49.5, 46.1, 30.3, 28.3, 28.0. HPLC t_R = 2.58 min (A). ES-MS m/z 358.3 $(M + H)^+$.

(1*S*,4′*S*)-[2-(1*H*-Indol-3-yl)-1-(4-*tert*-butyl-2-oxazolin-2-yl)-ethyl]-carbamic Acid *tert*-Butyl Ester 6{*8,3*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethyl-

amine (0.5 mL), reaction time 40 h. ^{1}H NMR ($CDCl_3$) δ_H: 8.88 (1H, bs), 7.48 (1H, dd, J = 5.5 Hz, J = 2.5 Hz), 7.08−6.99 (3H, m), 6.91 (1H, m), 5.22 (1H, d, J = 8.0 Hz), 4.64 (1H, dt, J = 8.0 Hz, J = 5.0 Hz), 4.24 (1H, t, J = 9.0 Hz), 4.16 (1H, t, J = 8.0 Hz), 3.62 (1H, dd, J = 9.0 Hz, J = 8.0 Hz), 3.29 (1H, dd, J = 14.5 Hz, J = 5.0 Hz), 3.19 (1H, dd, J = 14.5 Hz, J = 5.0 Hz), 1.43 (9H, s). ^{13}C NMR ($CDCl_3$) δ_C: 167.0, 155.1, 136.2, 127.6, 123.0, 121.8, 118.9, 118.1, 111.4, 109.3, 79.8, 75.2, 69.5, 49.1, 33.6, 28.3, 27.7, 25.6. HPLC t_R = 4.49 min (A). ES-MS m/z 386.3 $(M + H)^+$.

(1*R*,4′*R*)-[2-(1*H*-Indol-3-yl)-1-(4-phenyl-2-oxazolin-2-yl)-ethyl]-carbamic Acid *tert*-Butyl Ester 6{*9,1*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 16 h. ^{1}H NMR ($CDCl_3$) δ_H: 8.82 (1H, bs), 7.83 (1H, d, J = 7.5 Hz), 7.55−7.47 (4H, m), 7.44−7.28 (4H, m), 7.15 (1H, s), 5.50 (1H, d, J = 7.5 Hz), 5.18 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 5.07 (1H, m), 4.86 (1H, dd, J = 10.0 Hz, J = 8.5 Hz), 4.36 (1H, t, J = 8.5 Hz), 3.57 (2H, d, J = 5.0 Hz), 1.67 (9H, s). ^{13}C NMR ($CDCl_3$) δ_C: 168.0, 155.2, 141.8, 136.1, 128.6, 127.8, 127.5, 126.6, 123.0, 121.9, 119.3, 118.4, 111.3, 109.8, 79.8, 75.4, 69.2, 49.7, 30.3, 28.3. HPLC t_R = 2.95 min (A). ES-MS m/z 406.4 $(M + H)^+$.

(1*R*)-[2-(1*H*-Indol-3-yl)-1-(4,4-dimethyl-2-oxazolin-2-yl)-ethyl]-carbamic Acid *tert*-Butyl Ester 6{*9,2*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (1 mL), reaction time 40 h. ^{1}H NMR ($CDCl_3$) δ_H: 8.28 (1H, bs), 7.56 (1H, d, J = 7.5 Hz), 7.30 (1H, d, J = 7.5 Hz), 7.17−7.04 (6H, m), 6.96 (1H, s), 5.22 (1H, d, J = 7.0 Hz), 4.64 (1H, m), 3.91 (1H, d, J = 8.0 Hz), 3.85 (1H, d J = 8.0 Hz), 3.26(2H, m), 1.41 (9H, s), 1.12 (3H, s), 0.89 (3H, s). ^{13}C NMR ($CDCl_3$) δ_C: 164.7, 155.0, 136.0, 128.0, 122.0, 121.8, 119.3, 118.9, 111.0, 110.2, 79.5, 66.9, 49.5, 46.1, 30.3, 28.3, 28.0. HPLC t_R = 2.58 min (A). ES-MS m/z 358.3 $(M + H)^+$.

(1*R*,4′*S*)-[2-(1*H*-Indol-3-yl)-1-(4-*tert*-butyl-2-oxazolin-2-yl)-ethyl]-carbamic Acid *tert*-Butyl Ester 6{*9,3*}. This product was prepared according to the general procedure. The cyclization was performed in the presence of triethylamine (0.5 mL), reaction time 40 h. ^{1}H NMR ($CDCl_3$) δ_H: 8.18 (1H, bs), 7.57 (1H, d, J = 8.0 Hz), 7.29 (1H, d, J = 8.0 Hz), 7.14 (1H, td, J = 7.5 Hz, J = 1.0 Hz), 7.07 (1H, t, J = 7.5 Hz), 6.98 (1H, d, J = 2.0 Hz), 5.29 (1H, d, J = 7.0 Hz), 4.69 (1H, m), 4.19 (1H, t, J = 9.0 Hz), 3.90 (1H, t, J = 9.0 Hz), 3.74 (1H, t, J = 9.0 Hz), 3.32 (1H, dd, J = 14.5 Hz, J = 5.0 Hz), 3.22 (1H, dd, J = 14.5 Hz, J = 4.5 Hz), 1.42 (9H, s). ^{13}C NMR ($CDCl_3$) δ_C: 166.0, 155.0, 136.0, 128.1, 123.0, 121.8, 119.3, 119.1, 111.0, 110.5, 79.5, 75.4, 69.2, 49.9, 33.1, 28.1, 28.0, 25.6. HPLC t_R = 4.50 min (A). ES-MS m/z 386.3 $(M + H)^+$.

General Procedure for the Preparation of 2,4,5-Trisubstituted Oxazoline Preparation Using Resin 1b. The carboxylic acid **2** (0.07 mmol), amino alcohol **3** (0.09 mmol) and TEA (30 μL, 0.22 mmol) were placed in a microwave vial together with anhydrous THF (3 mL). Resin **1a** (120 mg, 0.15 mmol) was added, and the mixture was stirred vigorously for 1 h. Resin **1b** (120 mg, 0.15 mmol) and TEA (0.5 mL) were added, and the mixture was stirred at room temperature for 1 h, followed by heating under microwave irradiation at 120 °C for 10 min. The resin was removed by filtration, and the filtrates were passed through an amino-functionalized SPE column (Isolute NH_2 SPE column, 2 g). The resin and SPE column were washed with 15 mL of DCM, then the combined filtrates were evaporated under vacuum to afford the desired 2-oxazolines **6**, which were analyzed without further purification.

(4*S*,5*S*)-4-Methyl-2,5-diphenyl-2-oxazoline 6{*1,5*}. This product was prepared according to the general procedure. ^{1}H NMR ($CDCl_3$) δ_H: 8.01 (2H, m), 7.52−7.29 (8H, m), 5.09 (1H, d, J = 7.0 Hz), 4.20 (1H, quintet, J = 7.0 Hz), 1.48 (3H, d, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 162.8, 140.5, 131.4, 128.8, 128.4, 128.4, 128.3, 127.7, 125.6, 88.2, 70.9, 21.4. HPLC t_R = 2.42 min (A). ES-MS m/z 238.3 $(M + H)^+$.

(4*S*,5*S*)-4-Methyl-2-(4-nitrophenyl)-5-phenyl-2-oxazoline 6{*2,5*}. This product was prepared according to the general procedure. ^{1}H NMR ($CDCl_3$) δ_H: 8.55 (2H, d, J = 8.5 Hz), 8.45 (2H, d, J = 8.5 Hz), 7.70−7.58 (5H, m), 5.42 (1H, d, J = 8.5 Hz), 4.54 (1H, dq, J = 8.5 Hz, J = 6.5 Hz), 1.78 (3H, d, J = 6.5 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 160.9, 149.5, 139.7, 133.6, 129.3, 128.9, 128.6, 125.6, 123.6, 88.8, 71.2, 21.2. HPLC t_R = 3.73 min (A). ES-MS m/z 283.3 $(M + H)^+$.

(4*S*,5*S*)-2-(2-Methoxyphenyl)-4-methyl-5-phenyl-2-oxazoline 6{*4,5*}. This product was prepared according to the general procedure. ^{1}H NMR ($CDCl_3$) δ_H: 7.82 (1H, dd, J = 8.0 Hz, J = 2.0 Hz), 7.46−7.29 (6H, m), 7.01−6.95 (2H, m), 5.05 (1H, d, J = 8.5 Hz), 4.23 (1H, dq, J = 8.5 Hz, J = 6.5 Hz), 3.92 (3H, s), 1.49 (3H, d, J = 6.5 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 161.4, 158.6, 140.8, 132.3, 131.4, 128.7, 128.1, 125.6, 120.2, 117.0, 111.6, 87.3, 71.3, 56.1, 21.5. HPLC t_R = 2.47 min (A). ES-MS m/z 268.3 $(M + H)^+$.

(4*S*,5*S*)-4-Methyl-2-(4-nitrophenylpropyl)-5-phenyl-2-oxazoline 6{*7,5*}. This product was prepared according to the general procedure. ^{1}H NMR ($CDCl_3$) δ_H: 8.41 (2H, d, J = 9.0 Hz), 7.68−7.58 (5H, m), 7.55−7.51 (2H, m), 5.16 (1H, d, J = 7.5 Hz), 4.27 (1H, quintet, J = 7.5 Hz), 3.10 (2H, t, J = 8.0 Hz), 2.67 (2H, t, J = 8.0 Hz), 2.33 (2H, quintet, J = 8.0 Hz), 1.64 (3H, d, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 165.8, 149.3, 146.4, 140.3, 129.3, 128.8, 128.3, 125.5, 123.7, 88.0, 70.3, 35.0, 27.5, 27.1, 21.5. HPLC t_R = 4.58 min (B). ES-MS m/z 325.3 $(M + H)^+$.

(4*S*,5*R*)-2-Phenyl-3a,4,5,6,7,7a-hexahydrobenzoxazole 6{*1,6*}. This product was prepared according to the general procedure. ^{1}H NMR ($CDCl_3$) δ_H: 7.93 (2H, d, J = 8.0 Hz), 7.46−7.35 (3H, m), 4.66 (1H, dt, J = 8.0 Hz, J = 5.0 Hz), 4.11 (1H, dt, J = 8.0 Hz, J = 6.5 Hz), 1.95−1.35 (8H, m). ^{13}C NMR ($CDCl_3$) δ_C: 164.2, 131.2, 128.4, 128.2, 128.1, 78.8, 63.5, 27.7, 26.2, 19.8, 19.1. HPLC t_R = 1.63 min (A). ES-MS m/z 202.4 $(M + H)^+$.

(4*S*,5*S*)-4-Methoxymethyl-2,5-diphenyl-2-oxazoline 6{*1,8*}. This product was prepared according to the general procedure, except that the cyclization was performed at room temperature (reaction time 3 days). Around 7 mol % of uncyclized intermediate could be observed by 1H NMR. ^{1}H NMR ($CDCl_3$) δ_H: 8.00 (2H, d, J = 8 Hz), 7.46−7.18 (8H,

m), 5.75 (1H, d, $J = 10.0$ Hz), 4.62 (1H, dt, $J = 10.0$ Hz, $J = 6.0$ Hz), 3.23 (1H, dd, $J = 9.5$ Hz, $J = 6.0$ Hz), 2.93 (1H, covered under singlet at 2.92), 2.92 (3H, s). ^{13}C NMR ($CDCl_3$) δ_C: 166.4, 136.4, 131.6, 128.5, 128.4, 128.1, 128.0, 127.4, 126.4, 82.9, 72.2, 69.8, 58.7. HPLC $t_R = 2.67$ min (A). ES-MS m/z 268.3 $(M + H)^+$.

Supporting Information Available. Copies of ^{1}H and ^{13}C NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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